IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Applicant	:	Gunter Fuhr	On Appeal to the Board of Appeals and Interferences
Serial No.	:	09/582,609	
Filed	:	September 6, 2000	Examiner: Padmanabhan, K.
For	:	PROCESS AND DEVICES TO MEASURE, CALIBRATE AND USE LASER TWEEZERS	Art Unit: 1641

BRIEF ON APPEAL

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December 9, 2003
Date of Deposit

James J. Maune	26,946
Attorney Name	Registration No.
Signature	December 9, 2003
	Date of Signature

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

STATUTE(S)

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BRIEF ON APPEAL

I. REAL PARTY IN INTEREST

This application has been assigned by the inventors Gunter Fuhr, Thomas Schnelle, Torsten Muller, Hermine Hitzler, Karl-Otto Greulich, and Shamci Monajembashi to Evotec Biosystems AG, who is the real party in interest.

II. RELATED APPEALS AND INTERFERENCES

The applicant and the applicant's legal representatives are unaware of any appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

Claims 28-30, 32-36, 39-44 and 53-54 have been rejected under 35 U.S.C. §102(b) as being anticipated by K. Morishima et al., Proc. of IEEE (1997) (Morishima et al.). Claim 31 has been rejected under 35 U.S.C. §103(a) as being obvious in view Morishima et al. further in view of K. Svoboda, Ann. Rev. Biophys. Biomol. Struc., 90, 209 (1994) (Svoboda).

Claims 38 and 45-52 have been rejected under 35 U.S.C. §103(a) as being obvious in view of Morishima et al. further in view of G. Fuhr et al., Biochim. Biophys. Acta., 1201, 353 (1994) (Fuhr et al.). No claims are allowed.

Appellant appeals from the Final Rejection of pending claims 29-36, 38-43, 45-51, 53, 55 and 56. The pending claims are set forth in the Appendix to this brief.

IV. STATUS OF AMENDMENTS

No new amendments have been requested.

V. SUMMARY OF INVENTION

Applicant's invention concerns a method and device for exerting optically induced forces on at least one particle situated at the focal point of an optical cage. In addition, electric field forces are generated that contain electric field gradients that form a capture area acting on the particle (or particles). The minimum level of the electrical field forces corresponds to the capture area. The minimum level of optically-induced forces is the focus of the optical cage. Between both minimum levels is a field barrier that depends on the amplitude of the effective electrical fields, the light power of the optical cage, and the distance between the minimum levels. Movement of a particle within a microelectrode arrangement from the focal point of the optical cage to the capture zone of a three-dimensional electrical field, or vice versa, can be induced by varying the amplitude of the electric field, the light output and/or the distance between the capture zone and the focal point.

In particular, the invention provides capturing at least one microscopic particle in the focus of an optical cage in a microelectrode arrangement and positioning it with reference to a separate electrical capture area (or capture point), which is formed by electrical field gradients in the microelectrode arrangement. The focus of the optical cage with the particle is initially

positioned at a distance from the capture area, i.e., at a distance from the minimum electrical field level of the capture area that represents an electrical field cage. Then the field forces in the optical cage and/or in the electrical capture area and/or the distance between the optical cage and electrical capture area are varied until the particle moves from the focus to the capture area or vice versa.

VI. ISSUES ON APPEAL

The issues on appeal are as follows:

A. whether the Examiner failed to establish a *prima facie* case that claims 29-36, 38-43, 45-51, 53, 55, and 56, which stand rejected under 35 U.S.C. § 102(b), are anticipated by the Morishima et al. reference;

B. whether the Examiner failed to establish a *prima facie* case that claim 31, which stands rejected under 35 U.S.C. § 103(a), is unpatentable over the Morishima et al. reference in view of the Svoboda reference;

C. whether the Examiner failed to establish a *prima facie* case that claims 38 and 45-51, which stand rejected under 35 U.S.C. § 103(a), are unpatentable over the Morishima et al. reference in view of the Fuhr et al. reference.

VII. GROUPING OF THE CLAIMS

For purposes of this appeal, the claims are grouped as follows:

Group 1: Claims 29-36, 38-43, 45-51, 53, 55 and 56 stand or fall together.

VIII. ARGUMENT

A. Relevant Legal Standards

In order to render a claim anticipated under 35 U.S.C. § 102, a single prior art reference must disclose each and every element of the claim in exactly the same way.

See Lindeman Machinenfabrik v. Am Hoist and Derrick, 730 F.2d 1452, 1458 (Fed. Cir. 1984), emphasis added; *see Tights, Inc. v. Acme-McCrary Corp.*, 541 F.2d 1047, 191 U.S.P.Q. 305 (4th Cir. 1976); *see also Shanklin Corp. v. Springfield Photo Mount Co.*, 521 F.2d 609, 187 U.S.P.Q. 129 (1st Cir. 1975).

"A prior art publication cannot be modified by the knowledge of those skilled in the art for purposes of anticipation." *In re Saunders*, 444 F.2d 599, 602-03, 170 U.S.P.Q. 213 (C.C.P.A. 1971); *see also Studiengesellschaft Kohle mbH v. Dart Indus.*, 549 F.Supp. 716, 216 U.S.P.Q. 381 (D. Del. 1982), *aff'd* 726 F.2d 724, 220 U.S.P.Q. 841 (Fed. Cir. 1984). It must be "clear that the missing descriptive matter is necessarily present in the ... reference." *See Acromed Corp. v. Sofamor Danek Group, Inc.*, 253 F.3d 1371, 1383 (Fed. Cir. 2001), *citing Continental Can Co. USA Inc. v. Monsanto Co.*, 948 F.2d 1264, 1268-69, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991).

"To reject claims in an application under Section 103, an examiner must show an unrebutted *prima facie* case of obviousness." *In re Rouffet*, 47 U.S.P.Q.2d 1453, 1455 (Fed. Cir. 1998). The Supreme Court in *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966), stated:

> Under Section 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined.

Indeed, to sustain a rejection under 35 U.S.C. § 103(a), there must be some teaching, other than the instant application, to alter the prior art to arrive at the claimed invention. "The problem confronted by the inventor must be considered in determining whether it would have been obvious to combine the references in order to solve the problem." *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 679 (Fed. Cir. 1998).

Thus, to establish a *prima facie* case of obviousness, the Examiner has an obligation to construe the scope of the prior art, identify the differences between the claims and the prior art, and determine the level of skill in the pertinent art at the time of the invention. From this, the Examiner must provide a positive reason why it would be obvious to modify the prior art to arrive at the claimed invention. Absent an explanation of "the specific understanding or principle within the knowledge of a skilled artisan that would motivate one with no knowledge of [applicant's] invention to make the combination, [there is an inference] that the examiner selected these references with the assistance of hindsight," which is clearly impermissible. *In re Rouffet*, 47 U.S.P.Q.2d 1453, 1458 (Fed. Cir. 1998). A positive suggestion or motivation to alter the prior art is a requisite safeguard against hindsight being used to negate patentability. *Id.* at 1459.

"Multiple cited prior art references *must suggest the desirability* of being combined and the reference must be viewed without the benefit of *hindsight* afforded to the disclosure. *In re Paulsen*, 30 F.3d 1475, 1482 (Fed. Cir. 1994); *emphasis added.* "It is improper to use the inventor's disclosure as a road map for selecting and combining prior art disclosures." *See Grain Processing Corp. v. American Maize-Products Corp.*, 840 F.2d 902, 907 (Fed. Cir. 1988). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not be based on Appellant's disclosure. *See In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

When combining references for purposes of demonstrating obviousness of the claimed invention, the first requirement is that a suggestion, teaching, or motivation to combine the prior art references be shown. *C.R. Bard, Inc. v. M3 Sys. Inc.*, 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998). This showing is an "essential

evidentiary component of an obviousness holding." *Id.*, emphasis added. This evidence may flow from the (1) prior art references themselves, (2) the knowledge of one of ordinary skill in the art, or, in some cases, (3) from the nature of the problem to be solved. *Brown & Williamson Tobacco Corp. v. Philip Morris, Inc.*, 229 F.3d 1120, 1125 (Fed. Cir. 2000), *citing Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1630 (Fed.Cir. 1996). However, the suggestion more often comes from the teachings of the pertinent references. *See In re Rouffet*, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998). "This showing must be clear and particular, and broad conclusory statements about the teaching of multiple references, standing alone, are not "evidence." *Brown & Williamson Tobacco Corp. v. Philip Morris, Inc.*, 229 F.3d 1120, 1125 (Fed. Cir. 2000); emphasis added.

B. The Rejections

1. Issue A

Whether the Examiner failed to establish a *prima facie* case that claims 29-36, 38-43, 45-51, 53, 55, and 56, which stand rejected under 35 U.S.C. § 102(b), are anticipated by the Morishima et al. reference. It is alleged that Morishima et al. discloses a microchannel system for screening of E. coli, wherein the bacteria are manipulated by dielectrophoretic force and radiation pressure of a laser tweezer. To support the rejection, the Examiner notes that Morishima et al. combines optical trapping and electric forces for the manipulation of particles and isolation of one particle. The microelectrodes of the device induce dispersion of the bacteria, while the E. coli is three dimensionally optically trapped at the focal beam of the laser. Therefore, by controlling the magnitude of the electric field, the unneeded bacteria is separated. (*see* Morishima et al., at p 156).

However, as described in the introductory portion of the present application (*see* Specification), Morishima et al. describes the combination of optical and dielectrophoretic manipulation of microorganisms. First, one microorganism is selected from a group of microorganisms with a laser-tweezer. Then the remaining microorganisms are separated from the selected microorganism by dispersing the microorganisms to the border of the microelectrode arrangement using dielectrophoretic forces. (*see* Morishima et al., Figure 3). Therefore, Morishima et al. uses electrical fields for generating repelling forces only. Morishima et al. does not disclose an electrical field cage with a capture point.

In contrast, the present claimed invention recites the formation of a three-dimensional electrical capture area representing an electrical field cage with a capture point at a minimum electrical field level of the capture area. As shown in Figure 1 of the present application, the optical cage 110a and an electrical trap 110b are formed at a distance separated from each other. Morishima et al. combines an optical cage in the center of the microsystem with electric forces directed outwardly. This arrangement allows for the separation of a single trapped E. Coli in the center from the remaining parts of the sample as shown in Figure 2 of the Morishima et al. reference. Therefore, the electrical capture area of Morishima et al. is defined by the outer surroundings and, consequently, there is no minimum electrical field level at any capture point. Furthermore, Morishima et al. discloses that the particles "migrate toward the normal to the line of electric line and aggregate in the state of the pearl chain formation by dielectrophoretic force." (*see* Morishima et al., at page 156). This chain formation means that there is no particular capture point with a minimum electrical field level comparable with the electrical trap used in the present claimed invention.

Moreover, according to the present claimed invention, a particle trapped in one of the optical or electrical traps is moved between the optical cage and the electrical capture area (or vice versa) by varying operation parameters, i.e., the amplitude of the effective electrical fields, the light power of the optical cage, and the distance between the minimum levels. (*see* present application, claim 55; step c). This movement can be used to measure the optically induced forces or detect at least one condition of the parameters that causes the movement between the traps (*see* present application claim 55, step d). In contrast, Morishima et al. is directed at separation of a single particle from the remaining sample only. To achieve this separation, the remaining sample must be repelled from the selected particle into all surrounding directions. The technique of Morishima et al. would not work with the formation of an electrical trap with a single minimum on one side of the optical trap as the particles to be separated would not disperse.

Accordingly, Appellants respectfully request that the Board reverse the Examiner's rejection of claims 29-36, 38-43, 45-51, 53, 55, and 56, which stand rejected under 35 U.S.C. § 102(b), as anticipated by the Morishima et al. reference.

2. Issue B

Whether the Examiner failed to establish a *prima facie* case that claim 31, which stands rejected under 35 U.S.C. § 103(a), is unpatentable over the Morishima et al. reference in view of the Svoboda reference. Claim 31 depends from independent claim 55. Accordingly, claim 31 is believed to be patentable for at least the same reasons as provided above with reference to independent claim 55. Accordingly, Appellants respectfully request that the Board reverse the Examiner's rejection of claim 31 under 35 U.S.C. § 103(a), as unpatentable over the Morishima et al. reference in view of the Svoboda reference.

3. Issue C

Whether the Examiner failed to establish a *prima facie* case that claims 38 and 45-51, which stand rejected under 35 U.S.C. § 103(a), are unpatentable over the Morishima et al. reference in view of the Fuhr et al. reference. Claim 38 depends from independent claim 55. Accordingly, claim 38 is believed to be patentable for at least the same reasons as provided above with reference to independent claim 55. Claims 45-51, depends from independent claim 56. Independent claim 56 relates to a device to measure or exert optically-induced force capable to move or hold at least one particle in a focus of an optical cage, which includes substantially the same recitations as provided above with reference to independent claim 55. Therefore, claims 45-51 are believed to be patentable for at least the same reasons as provided above with reference to independent claim 55.

Accordingly, Appellants respectfully request that the Board reverse the Examiner's rejection of claims 38 and 45-51, under 35 U.S.C. § 103(a), as unpatentable over the Morishima et al. reference in view of the Fuhr et al. reference.

IX. CONCLUSION

For the reasons indicated above, Appellant respectfully submits that the invention recited in each of the claims of the present application as provided above is new and non-obvious. Reversal of the Examiner's rejections of the claims is therefore respectfully requested.

Respectfully submitted,

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APPENDIX TO BRIEF ON APPEAL

The pending claims are as follows:

--29. The process according to claim 55 in which a particle is placed in the focus or capture area to measure optically-induced forces, and the optically-induced forces are measured from the amplitude of the electrical field and the distance of the capture area from the focus when the particle moves from the focus to the capture area or vice versa.--

--30. The process according to claim 29 in which the optically-induced forces are repeatedly measured for all relevant directions in space corresponding to mutual alignment of said positions of said focus and said capture area.--

--31. The process according to claim 29 in which the optical cage is calibrated by determining a relationship between the light power to generate the optical cage and the forces induced on a particle in the optical cage.--

--32. The process according to claim 55 in which the distance between the focus and capture area is at least one-tenth of a particle diameter.--

--33. The process according to claim 55 in which the capture area is a capture point that is in a beam field of the optical cage so that the at least one particle moves back and forth between the

capture point and focus when the amplitude of one of the electrode signals and light power is varied, and an associated value of the amplitude is used to measure the optically-induced forces.-

--34. The process according to claim 55 in which numerous particles are sequentially injected with said optical cage into said capture area, wherein said particles are positioned in predetermined positions within the capture area relative to other particles in the capture area.—

--35. The process according to claim 55 in which the light beam of the optical cage is adjusted and one of a capture quality and symmetry of the optical cage are measured.--

--36. The process according to claim 55 in which passive electric properties of said at least one particle are characterized based on the measured optically-induced forces.--

--38. The process according to claim 55 in which an electrode of the microelectrode arrangement is alternatively supplied with at least one of signals phase-shifted 180° and rotation-generating signals with a predetermined phase division.--

--39. The process according to claim 55 in which at least one field barrier is formed between said capture point and said optical cage.--

--40. The process according to claim 55 in which a particle movement is detected by one of optical and electrical detection.--

--41. The process according to claim 55 in which the particles are synthetic or natural particles with a size less than 200 μm.--

--42. The process according to claim 55 in which the particles are biological cells or their components.--

--43. The process according to claim 55 in which the movement of the particle between the capture area and the focus is used to adjust the optical cage.--

--45. The device according to claim 56 in which the microelectrode arrangement comprises flat electrodes that are in groups on two spaced substrates of which at least one is transparent.--

--46. The device according to claim 45 in which the transparent substrate is has a thickness of less than 500 μm.--

-- 47. The device according to claim 45 in which the electrodes are attached to facing surfaces of the substrates, and the substrates are separated from each other by a spacer that forms a

suspension area into which the focus of the optical cage can be coupled by the illumination device through one of the two substrates.--

-- 48. The device according to claim 47 in which the suspension area is part of a channel structure through which the particles are introduced by means of a flow of solution into the field of the microelectrode arrangement.--

--49. The device according to claims 56 in which the microelectrode arrangement comprises electrodes that are set up to generate a multiple field with an electrical field distribution symmetrical in at least one of the x, y and z direction.--

--50. The device according to claim 56 in which the electrodes are coated with a layer of one of an insulating material, dielectric or a metal, which layer is essentially inert to a suspension liquid in the fluid microsystem.--

--51. The device according to claim 50 in which the electrodes consist of platinum, titanium, tantalum or gold.--

--53. Calibrating a laser tweezer by exerting optically-induced forces on at least one particle and measuring said forces with a procedure according to claim 55.--

-- 55. A procedure to exert or measure optically-induced forces which are capable of moving at least one particle or holding at least one particle in a focus of an optical cage formed with a light beam, comprising:

a) positioning the focus in a microelectrode arrangement in which an electrical field is formed that has a field gradient which forms a three-dimensional electrical capture area, said electrical capture area representing an electrical field cage with a capture point at a minimum electrical field level of the capture area, wherein the focus is positioned at a distance from the capture point

b) positioning said at least one particle at one of the focus and the capture point,

c) varying at least one parameter selected from an amplitude of said electrical field, a light power of said light beam and the distance of the capture point from the focus until the particle moves between the focus and the capture area, and

d) exerting said optically-induced forces, wherein said at least one particle is at least temporarily moved between the focus and the capture area, or measuring said optically-induced forces, wherein said at least one parameter varied in step c) is detected when said at least one particle moves between the focus and the capture point.--

--56. A device to measure or exert optically-induced forces which are capable to move or hold at least one particle in a focus of an optical cage formed with a light beam that comprises:

-a fluid microsystem with a microelectrode arrangement that is set up to form an electrical field that has a field gradient which forms a three-dimensional electrical capture area,

said electrical capture area representing an electrical field cage with a capture point at a minimum electrical field level of the capture area,

-an illuminating device that is set up to emit a laser beam forming an optical cage in the microelectrode arrangement of the microsystem, and

-a monitoring and/or detection device to optically measure a movement of said at least one particle in the microelectrode arrangement.--